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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/812,065 | 03/19/2001 | Joel S. Rossier | JYG106USA | 9003 |

270 7590 07/14/2004

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| EXAMINER | |
|---|---|
| MUTSCHLER, BRIAN L | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1753 | |

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/812,065 | ROSSIER ET AL. | |
| | Examiner | Art Unit | |
| | Brian L. Mutschler | 1753 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *03 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-9 and 11-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 11-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Comments*

1. Applicant's cancellation of claim 10 and addition of claims 13 and 14 is acknowledged.

2. The objection to the abstract and the specification has been overcome by Applicant's amendment.

3. The rejection of claims 9-11 under 35 U.S.C. 112, second paragraph, has been overcome by Applicant's amendment.

4. The rejections of the claims under 35 U.S.C. 103 set forth in the prior Office action have been modified in response to Applicant's amendments to the claims, which now require at least 8 ports on the multi-port valve, which acts as the sole actuator.

### *Claim Rejections - 35 USC § 103*

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-9, 11, 13, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ramsey (U.S. Pat. No. 5,858,195) in view of Knapp et al. (U.S. Pat. No. 6,235,471), Taylor et al. (U.S. Pat. No. 6,375,817), and Sklar et al. (U.S. Pat. No. 6,315,952).

Regarding claim 1, Ramsey teaches a micro-analytical apparatus for manipulating fluid samples comprising a substrate with a covered channel and openings at each of the channels (figs. 1, 2 and 31A-31C). The channels intersect to form a common intersection **40** (figs. 1 and 31A-31C). An electrokinetic valve and flow control system are connected to the end of each channel using electrodes, and the system acts as a valve to selectively control the volume of material transported through the intersection using electrophoretic and electroosmotic flow (col. 4, lines 6-30; col. 9, lines 25-40).

Regarding claim 2, the substrate is made of glass, crystalline quartz, fused quartz, fused silica, plastics, and silicon (col. 8, lines 21-36).

Regarding claim 3, the channels are covered with a cover plate that is bonded by a thermal bonding process (col. 8, lines 44-50). It is noted that the additional structural limitations of claim 3 consist only of a cover over the channels; the method by which the cover is affixed to the substrate does not limit the structure of the device.

Regarding claim 4, as shown in Figure 1, all of the openings at the ends of the channel are connected to the flow control system (fig. 1).

Regarding claim 5, a detection region is located along the channels (col. 10, lines 36-41; col. 16, line 47+).

Regarding claim 6, the detection region consists of electrodes or a window for spectroscopic detection, as evidenced by the fluorescence images shown in figure 8(b) (col. 16, line 47+).

Regarding claim 7, the channels may be attached to a detection device (col. 16, line 47+).

Regarding claim 8, Ramsey discloses a method of manipulating fluid samples in the apparatus comprising the steps of:

a. Pumping solvent (eluent) from reservoirs **12** and **14** located at the ends of channels **26** and **28** (comprising the first channel with channel **34**) through the intersection **40** while pressure is applied to channels **30** and **32** (second channel) (fig. 31C). While it is noted that Figure 31C is the "Finish" of the process as shown in the sequence of the three figures, Ramsey teaches that the process repeats and injects a second sample as a first sample is in channel **34**, thus making Figure 31C the first step in the manipulation of the second sample.

b. Switching the control system to a second position so that a sample solution is pumped from the analyte reservoir **16** into channel **30** (second channel) while pressure is applied to the other three openings (fig. 31A).

c. Switching the control system back to the original position so that the sample is pushed from channel **30** (second channel) through the intersection **40** and along channel **34** (first channel) (fig. 31B).

Regarding claim 9, an electric field is applied in the channels to sustain the flow of liquid during the method (fig. 32).

Regarding claim 11, the sample is pushed using electroosmotic or electrokinetic flow (col. 9, lines 35-40).

The apparatus and method of Ramsey differs from the instant invention because Ramsey does not teach the following:

a. A multi-port valve, as recited in claim 1. (Ramsey teaches an electrokinetic valve.)

b. The eluent solution is mechanically pumped, as recited in claim 8.

c. The manipulation of the fluid samples uses steps of switching the multi-port valve, as recited in claim 8.

d. The multi-port valve is switchable between first and second positions, as recited in claims 13 and 14.

Regarding claims 1 and 8, Knapp et al. disclose a micro-analytical system and methods for using the systems. Knapp et al. teach that material transport systems for moving fluid samples through microfluidic channels include "electrokinetic, electroosmotic, and electrophoretic systems (e.g., electrodes in fluidly connected wells having a coupled current and/or voltage controller), as well as micro-pump and valve systems" (col. 10, lines 12-19).

Taylor et al. describe a mechanical sample injection method for use in a microchip assembly having intersecting channels, wherein the injection method comprises similar flow patterns as taught by Ramsey (see figs. 2A-3F of US '817). Taylor et al. further teach the use of pressure-driven flow, which avoids the formation of electrolysis products generated in electrokinetic flow systems (col. 1, line 51 to col. 2, line 58). A pressure control device that includes valves, manifolds, tubing, and the like

is used to control the pressure driven flow within the channels (col. 5, lines 16-38). A potential is applied to electrophoretically move the sample (col. 7, lines 11-27).

Sklar et al. describe a method of using pressure-driven flow to inject a plurality of samples in channels for screening (figs. 1 and 2; col. 5, lines 41-53). Sklar et al. further teach the use of an 8-port valve to control the injection of the sample into the two channels, wherein each end of the channels is connected to the multi-port valve (figs. 1 and 2; col. 3, line 63 to col. 4, line 3). The multi-port valve is the sole controller for the direction of flow within the channels (figs. 1 and 2). With regard to claims 13 and 14, the multi-port valve is switchable between two positions to control the flow of the sample within the channels (figs. 1 and 2).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the electrokinetic valve in the apparatus and electrokinetic flow of Ramsey to use pressure-driven flow as taught by Knapp et al. and Taylor et al. because Knapp et al. teach that electrokinetic control systems and micro-pump and valve systems (i.e., pressure-driven systems) are equivalent means to control flow through channels in microfluidic devices, and Taylor et al. further teach that pressure-driven flow is desirable for sample injection and analysis because it prevents the formation of electrolysis products generated in electrokinetic systems.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have further modified the system and method of Ramsey to use a multi-port valve as taught by Sklar et al. because multi-port valves simplify the operation of fluid transport systems by manipulating a plurality of ports with a single

valve. The connection of such multi-port valves would have been obvious to one having ordinary skill in the art at the time the invention was made because the routing of conduits and control valves is routine in the art of microfluidics. As demonstrated by Taylor et al., a microfluidic system comprising two intersecting channels and using pressure-driven flow must be connected to a pressure source at a minimum of three ends of the channels (see figs. 2A-3F of US '817).

7. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ramsey (U.S. Pat. No. 5,858,195) in view of Knapp et al. (U.S. Pat. No. 6,235,471), Taylor et al. (U.S. Pat. No. 6,375,817), and Sklar et al. (U.S. Pat. No. 6,315,952), as applied above to claims 1-9, 11, 13, and 14, and further in view of Parce et al. (U.S. Pat. No. 6,458,259).

Ramsey, Knapp et al., Taylor et al., and Sklar et al. describe an apparatus and method having the limitations recited in claims 1-9, 11, 13, and 14 of the instant invention, as explained above in section 6.

The apparatus and method described by Ramsey, Knapp et al., Taylor et al. and Sklar et al. differs from the instant invention because they do not disclose that at least part of the first or second channel contains a stationary phase in order to perform chromatography, electrochemistry, electrophoresis, immunological or enzymatic analysis or any combination thereof, as recited in claim 12.

Parce et al. disclose a micro-analytical apparatus and method using both mechanical and electrical flow through the channels. Parce et al. teach that the channels may optionally contain a gel (stationary phase) (col. 4, lines 38-42).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the method described by Ramsey, Knapp et al., Taylor et al., and Sklar et al. to use a stationary phase as taught by Parce et al. because stationary phase allows for a greater separation in components in electrophoretic separations.

***Response to Arguments***

8. Applicant's arguments filed May 3, 2004, have been fully considered but they are not persuasive.

9. Applicant's arguments center around the differences between electrokinetic and mechanical pumping for the injection of samples into channels (e.g., see page 16 of Applicant's response). As explained above, Ramsey teaches the same flow patterns as the method of the instant claims (see figs. 31A-31C of US '195). The difference between the pinched injection of Ramsey and the instant claims is the use of mechanical pumping as opposed to electrokinetic pumping. In general, Knapp et al. teaches that electrokinetic flow is equivalent to micro-pumping and valve systems. Taylor et al. disclose the use pressure-driven systems for the injection of samples into a channel (see figs. 2A-3F of US '817). Taylor et al. teach that pressure-driven pumping is preferable to electrokinetic pumping because the mechanical pumping avoids the

generation of electrolysis products. Therefore, one skilled in the art would have been motivated to perform pinched injection using mechanical pumping. Furthermore, Sklar et al. teach the injection of samples into channels using the combination of pressure-driven flow and a multi-port valve to regulate the pressure within the channels (see figs. 1 and 2 of US '952). It is noted that multi-port valves are commonly used in analytical systems. Based on the teachings of Ramsey (electrokinetic valve), Knapp et al. (electrokinetic flow = micro-pumps and valve systems), Taylor et al. (pressure-driven injection with valve control system), and Sklar et al. (pressure-driven injection with multi-port valves), it would have been obvious to one skilled in the art to use a multi-port valve to perform pressure-driven pinched injection of a sample into channels.

Although not explicitly taught by the combination of references, the connection of the channels to a multi-port valve would have been obvious to one skilled in the art based upon the teachings of the prior art and the knowledge of one skilled in the art. As shown by Taylor et al., at least three ends of the channels must be connected to a pressure source to perform the sample injection (see figs. 2A-3F of US '817). Sklar et al. further show the connection of all four ends of two channels to a multi-port valve (see figs. 1 and 2 of US '952). Based on these teachings and the level of skill in the art required to make and use such an apparatus, the specific connections between the multi-port valve and the channels would have been obvious to a skilled artisan.

***Conclusion***

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian L. Mutschler whose telephone number is (571) 272-1341. The examiner can normally be reached on Monday-Friday from 7:30am to 4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BLM
July 9, 2004

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